

Serial No. 09/805,483  
Filed March 13, 2001  
Response to Office Action

#### REMARKS

All of the rejections in the previous Office Action have been repeated and all rejections are again traversed. Claims 39-50 are cancelled in this amendment and the rejections limited to these claims are thus moot (the rejections of paragraphs 7 and 9 of the Office Action).

Claims 1 and 10 are rejected as anticipated by U.S. Patent No. 4,863,972 to Itagaki et al. (the "972 patent"). Claims 1, 5, and 8-10 are rejected as anticipated by Thanoo (J. Pharm. Pharmacol. 1993) ("Thanoo 1993"). Claims 1, 5, 8, 10, and 11 are rejected as anticipated by Thanoo (J. Applied Biomat. 1991) ("Thanoo 1991"). Claims 6, 12, and 13 are rejected as obvious over either Thanoo 1991 or 1993 in view of U.S. Patent No 6,265,509 to Muller (the "509 patent").

#### The rejection of claims 1 and 10 as anticipated by the '972 patent

Claim 1 is for a microparticle that is formed from macromers having a polymeric backbone comprising units having a 1,2-diol or 1,3-diol structure and at least two pendant chains bearing crosslinkable groups. Claim 10 further states that the microparticle is biodegradable. Claim 1 has been amended solely to expedite prosecution to incorporate the element of claim 12 that the crosslinkable groups are crosslinked via free radical polymerization. Applicants do not agree that claim 1 prior to this amendment was taught by the prior art.

The '972 patent teaches crosslinking PVA with glutaraldehyde- a well-known method of crosslinking PVA. Regular PVA as used in the '872 patent simply has hydroxyl groups and does not have "pendant groups which are crosslinkable" as required by the instant claims. Pendant groups are described in the specification at page 5, lines 4-6: "The pendant chains are attached via the hydroxyl groups of the backbone. Desirably, the pendant chains having crosslinkable groups are attached via cyclic acetal linkages to the 1,2-diol or 1,3-diol hydroxyl groups." Also see page 4, lines 28-31- "The macromers have at least two pendant chains containing groups that can be crosslinked. The term group includes single polymerizable moieties, such as an acrylate, as well as larger crosslinkable regions, such as oligomeric or polymeric regions."

It is clear that the term "pendant chains with crosslinkable groups" does not include a simple -OH group. The pendant groups are attached via the hydroxyl groups and thus are not

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the hydroxyl groups- they are something attached to the hydroxyl groups. Nonetheless, to expedite prosecution, Applicants' have amended claim 1 to include the element that the crosslinkable groups are crosslinked using free radical polymerization- an element which is also not taught by the '872 patent.

The rejection of claims 1, 5, and 8-10 as anticipated by Thanoo 1993 and claims 1, 5, 8, 10, and 11 as anticipated by Thanoo 1991

Both Thanoo references also teach PVA crosslinked with glutaraldehyde. The references do not teach using macromers having pendant crosslinkable chains, or where the crosslinkable groups are crosslinked via free radical polymerization. These rejections are respectfully traversed.

The rejection of claims 6, 12, and 13 as obvious over either Thanoo 1991 or 1993 in view of the '509 patent

This rejection is also respectfully traversed. As with the '317 patent discussed above, the '509 patent teaches moldings formed from macromers. Applicants acknowledge in the application that the macromers taught by Müller can be used in the claimed invention.

As the Examiner points out, Müller teaches that various moldings can be formed, such as "biomedical and ophthalmic mouldings, mouldings used in surgery, such as heart valves and artificial arteries, films and membranes". Such moldings are produced by introducing the prepolymer into a mould, crosslinking the prepolymer, and then removing the article from the mould.

As discussed above, the Thanoo references teach microspheres formed by polymerizing PVA with glutaraldehyde. They do not teach the use of a prepolymer (macromer). Glutaraldehyde crosslinked PVA particles have been used for a number of years. Thanoo teaches a similar material- formed into microspheres rather than irregularly shaped particles. A particular drawback of glutaraldehyde crosslinked PVA is that it forms tough, water insoluble particles (see Billmeyer, F.W. Jr; 'Textbook of Polymer Science', John Wiley & Son, Inc. Singapore, pp 391-395, 1984).

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The '509 patent does not teach making microspheres. The moldings that are described are articles formed using a mold. Microspheres are not made this way and the reference does not suggest making microspheres. Thanoo does not suggest microspheres made by crosslinking a prepolymer- i.e. a polymer having crosslinkable groups. Thanoo teaches only crosslinking PVA polymer using glutaraldehyde. The microspheres taught by Thanoo are very different from the claimed microspheres. For one thing, by using macromers, the use of glutaraldehyde is completely avoided and the resulting microspheres do not have residual glutaraldehyde.

The Examiner argues that the Applicants' have not shown any unexpected results with the particular crosslinking method claimed but this is untrue. As argued previously (and repeated above) Applicants avoid the use of glutaraldehyde. The method of crosslinking by joining pendant groups using free radical polymerization provides a cleaner product.

There is no suggestion found in either reference to combine their teachings, as is required to maintain a rejection of obviousness. The '509 patent nowhere suggests that the macromers could be used to make microspheres. Neither Thanoo suggests in any way that PVA microspheres could be made without using glutaraldehyde.

A Notice of Allowance is respectfully requested.

Respectfully submitted,

  
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Collen A. Beard

September 14, 2005

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